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09/207,188	12/08/1998	MILAN S. BLAKE	2016-4005US1	6452

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EXAMINER
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ART UNIT	PAPER NUMBER
1645	17

DATE MAILED: 01/11/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/207,188	Blake et al.
Examiner	**Art Unit**
S. Devi, Ph.D.	1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) [X] Responsive to communication(s) filed on *Oct 19, 2001*.

2a) [X] This action is **FINAL.** 2b) [ ] This action is non-final.

3) [ ] Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) [X] Claim(s) *80-93* is/~~are~~ pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) [ ] Claim(s) _____ is/are allowed.

6) [X] Claim(s) *80-93* is/~~are~~ rejected.

7) [ ] Claim(s) _____ is/are objected to.

8) [ ] Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) [ ] The specification is objected to by the Examiner.

10) [ ] The drawing(s) filed on _____ is/are objected to by the Examiner.

11) [ ] The proposed drawing correction filed on _____ is: a) [ ] approved b) [ ] disapproved.

12) [ ] The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) [ ] Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) [ ] All b) [ ] Some* c) [ ] None of:

1. [ ] Certified copies of the priority documents have been received.
2. [ ] Certified copies of the priority documents have been received in Application No. _____.
3. [ ] Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) [ ] Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) [ ] Notice of References Cited (PTO-892)
16) [ ] Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) [ ] Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) [ ] Interview Summary (PTO-413) Paper No(s). _____
19) [ ] Notice of Informal Patent Application (PTO-152)
20) [ ] Other:

DETAILED ACTION

Applicants' Amendment

1) Acknowledgment is made of Applicants' amendment filed 10/19/01 (paper no. 16) in response to the non-final Office Action mailed 06/12/01 (paper no. 14), which amendment has been entered.

Status of Claims

2) Claims 61-72 have been canceled via the amendment filed 10/19/01.

New claims 80-93 have been added via the amendment filed 10/19/01.

Claims 73-93 are pending in this application.

Claims 80-93 are under examination.

Prior Citation of Title 35 Sections

3) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

4) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Objection(s) Withdrawn

5) The objection to the description for Figure 1 made in paragraph 9(b) of the Office Action mailed 07/14/00 (paper no. 7) is withdrawn in light of Applicants' amendment to the specification.

Rejection(s) Moot

6) The rejection of claims 61-63, 68 and 69 made in paragraph 13 of the Office Action mailed 07/14/00 (paper no. 7) under 35 U.S.C § 102(b) as being anticipated by Reimer *et al.* (*Carbohydr. Res.* 232: 131-142, 1992) and maintained in paragraph 18 of the Office Action mailed 06/12/01 (paper no. 14), is moot in light of Applicants' cancellation of the claims.

7) The rejection of claims 61-72 made in paragraph 15 of the Office Action mailed 07/14/00 (paper no. 7) under 35 U.S.C § 103(a) as being unpatentable over Reimer *et al.* (*Carbohydr. Res.*

232: 131-142, 1992) in view of Jennings *et al.* (US 4,356,170) and Barnes *et al.* (WO 87/06590) and maintained in paragraph 18 of the Office Action mailed 06/12/01 (paper no. 14), is moot in light of Applicants' cancellation of the claims.

8) The rejection of claims 61-63, 68 and 69 made in paragraph 20 of the Office Action mailed 06/12/01 (paper no. 14) under 35 U.S.C § 103(a) as being unpatentable over Reimer *et al.* (*Carbohydr. Res.* 232: 131-142, 1992), is moot in light of Applicants' cancellation of the claims.

9) The rejection of claims 61-72 made in paragraph 21 of the Office Action mailed 06/12/01 (paper no. 14) under 35 U.S.C § 103(a) as being unpatentable over Reimer *et al.* (*Carbohydr. Res.* 232: 131-142, 1992) in view of Jennings *et al.* (US 4,356,170) and Barnes *et al.* (WO 87/06590), is moot in light of Applicants' cancellation of the claims.

10) The rejection of claims 61-72 made in paragraph 21 of the Office Action mailed 06/12/01 (paper no. 14) under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 26-33 of the U.S. Patent 5,866,135, is moot in light of Applicants' cancellation of the claims.

Applicants' Response

11) In the amendment filed 10/19/01, in response to the art rejection that is now rendered moot, Applicants state that they "have relied on the Examiners suggestion to recite a method of "eliciting a protective immune response in a mammal".' However, in the Office Action mailed 06/12/01, the Applicants' claim language, "method of immunizing an mammal" was discussed in relation to the Reimer's teaching of a method of immunization. The Applicants' claim language "method of immunizing an mammal" was also discussed in relation to the Applicants' remarks on the McCarty's statement about the "protective immunogenic response". Applicants were not suggested to 'recite a method of "eliciting a protective immune response"'.

Applicants state that the prior art applied previously, Reimer *et al.* (1992), "does not teach a method of immunizing a mammal against <u>infection</u> by group A Streptococci" [Emphasis in original], alleging basically that Reimer *et al.* are silent on the protective nature of the GASP antibodies elicited by their conjugates against group A streptococcal infection. See page 3 of the amendment filed 10/19/01. It should be noted that Reimer *et al.* did teach a method of eliciting

an anti-GASP immune response in a mammal by administering a conjugated GASP of formula I, wherein n=1 or n=2. In this regard, it should also be noted that the instant specification does not provide an enabling disclosure showing that the GASP antibodies elicited by Applicants' GASP conjugate(s) comprising the recited polysaccharide wherein, for example, n=1 or n=2, are 'protective' against group A streptococcal infection.

New Rejection(s)

12) Applicants are asked to note the new rejections made in this Office Action. Applicants' amendment, i.e., submission of new claims, necessitated the new grounds of rejections presented in this Office Action.

Double Patenting Rejection(s)

13) The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970) and *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 C.F.R 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 C.F.R 1.130(b).

Claims 80-93 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 26-33 of the U.S. Patent 5,866,135. Although the conflicting claims are not identical, they are not patentably distinct from each other, because of the overlapping scope. Furthermore, there is no apparent reason why Applicants were prevented from presenting claims corresponding to those of the instant application during the prosecution of the parent application which matured into US Patent 5,866,135. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

It is noted that Applicants have agreed to file a terminal disclaimer upon allowance of

claims in the instant application. See last paragraph on page 7 of Applicants' amendment filed 10/19/01.

Rejection(s) under 35 U.S.C. 112, Second Paragraph

14) Claims 80-93 are rejected under 35 U.S.C § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

(a) Claim 80 is indefinite and/or incorrect in the recitation "conjugate of formula (I)" (see line 3), because the formula (I) recited in claims 80 does not appear to be that of a conjugate, but of a polysaccharide component of the recited conjugate.

(b) Claim 80 lacks antecedent basis for the recitation "linked to protein or protein fragment" (see lines 4 and 5 below the formula). Since there is an earlier recitation of this limitation in the claim, for proper antecedence, it is suggested that Applicants replace the recitation with --linked to said protein or protein fragment--.

(c) Claim 80 is confusing in the recitation "protective response in the mammal" (see last line), because it is unclear what the difference is, if any, between this limitation and the limitation "protective immune response in a mammal" in line 1 of the claim. Clarification/ correction is requested.

(d) Claim 90 is indefinite and lacks antecedent basis for the recitation "the polysaccharide is administered with an adjuvant". Claim 90 depends from claim 81, which in turn depends from claim 80. What is recited to be administered to a mammal in claim 80 is a polysaccharide-protein or a polysaccharide-protein fragment "conjugate" as opposed to a "polysaccharide".

(e) Claim 93 is vague and confusing and/or lacks proper antecedent basis for the recitation "the group A polysaccharide". Claim 93 depends from claim 81, which in turn depends from claim 80. What is recited in claim 80 is a "group A streptococcal polysaccharide" as opposed to a "group A polysaccharide".

(f) Claim 93 is further confusing in the recitation "wherein the group A polysaccharide is administered in a dosage amount of about 0.1". Claim 93 depends from claim 81, which in turn depends from claim 80. What is recited as being administered in claim 80 is

the "conjugate", but not the polysaccharide. It is unclear whether the dosage recited in claim 93 represents the amount of the conjugate or the polysaccharide component of the conjugate.

(g) Claim 80 lacks proper antecedent basis for the recitation "the polysaccharide" (see line 2 below the formula), because there is an earlier recitation of a "polysaccharide protein ..... conjugate", but not of a polysaccharide.

(h) Claims 81-93, which depend directly or indirectly, from claim 80 are also rejected under 35 U.S.C § 112, second paragraph, as being indefinite because of the vagueness or indefiniteness identified above in the base claim.

Rejection(s) under 35 U.S.C. § 112, First Paragraph

15) Claims 80-93 are rejected under 35 U.S.C § 112, first paragraph, because the specification, while being enabling for a method of eliciting an immune response to group A streptococcal polysaccharide in rabbits comprising administering to rabbits an amount of a group A streptococcal polysaccharide-tetanus toxoid conjugate, wherein the polysaccharide is of formula I and has an average molecular weight of 10 Kd, does not reasonably provide enablement for a method of eliciting a 'protective' immune response in a mammal (including a rabbit, human or a human child) 'against infection by group A streptococcal bacteria' comprising administering such a conjugate, or a conjugate having the polysaccharide of formula I conjugated either to a protein or a fragment of a protein, wherein n is 'about 1 to about 50', or 'about 3 to about 30'. The specification does not enable any person skilled in the art to which it pertains, or with which it is most clearly connected, to make and/or use the invention commensurate in scope with these claims.

Instant claims are evaluated based on the *Wands* analysis. Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Circ. 1988) as follows:

- The quantity of experimentation necessary (time and expense);
- The amount of direction or guidance presented;
- The presence or absence of working examples of the invention;
- The nature of the invention;
- The state of the art;
- The relative skill of those in the art;
- The predictability or unpredictability of the art; and

- The breadth of the claims.

The instant claims are drawn to a method of eliciting a protective immune response in a mammal, including a human and a child, against infection by group A streptococcal bacteria by administering a conjugated polysaccharide of the recited formula I wherein n is a number sufficient to confer an average molecular weight to the polysaccharide "large enough to be protective". Thus, the breadth of the claims encompasses a method of administering to a mammal a conjugated GASP polysaccharide of formula I, wherein for example, n=1, n=2, n=3 etc., which elicits a "protective" immune response against group A streptococcal infection. The polysaccharide is conjugated to a protein, or a fragment of a protein. A review of the instant disclosure shows that no method of eliciting a "protective immune response" in any mammal, including a rabbit, human or a human child, "against infection by group A streptococcal bacteria" is enabled, which method comprises administering a protein or a protein fragment conjugated to the polysaccharide of formula I, wherein the average molecular weight of the polysaccharide is 10 Kd, or "large enough to be protective", or wherein n is 'about 1 to about 50' or 'about 3 to 30'. The instant specification does not disclose the precise average molecular weight of the group A streptococcal polysaccharide of formula I that is "large enough to be protective" in a mammal against infection by group A streptococcal bacteria. There is no data within the instant specification showing that an isolated group A streptococcal polysaccharide of any particular size or molecular weight on conjugation to a protein (let alone a protein fragment) does elicit a 'protective' immune response in any mammal, especially a human or human child, 'against infection by group A streptococcal bacteria'. The instant specification at Example 7 describes a method of administering rabbits with a native group A streptococcal polysaccharide (GASP) either uncoupled or conjugated to tetanus toxoid. Table IV shows that the native GASP did not elicit a GASP-specific antibody response after the first, second and third immunizations. On day 21 post first immunization, a saline solution of the GASP having an assumed molecular weight of about 10 Kd (i.e., n=about 20) and covalently coupled to tetanus toxoid induced the same base line titer of GASP antibodies (i.e., 100) in rabbits as that elicited by the uncoupled native GASP. This conjugate in saline elicited measurable GASP antibody titers by ELISA on days 42 and 52 post-immunization. When rabbits were immunized with the 10 Kd GASP conjugate admixed

with a clinically acceptable or unacceptable adjuvant such as aluminum hydroxide, ST adjuvant or Freund's adjuvant, higher levels of GASP antibodies were elicited. However, there is no showing within the instant specification, as originally filed, that the GASP-specific antibodies elicited by the 10 Kd GASP-tetanus toxoid conjugate of Example 7 are 'protective' 'against infection by group A streptococcal bacteria' in a mammal, including a human and a human child. No evidence is of record in the instant specification showing that a conjugate comprising a GASP of formula I having an average size wherein n is a number that falls anywhere in the broad range of 'about 1 to about 50' or 'about 3 to about 30' and wherein GASP is conjugated to a protein (let alone a protein fragment) elicits a 'protective immune response' in any mammal. Furthermore, there is no showing of elicitation of a 'protective' immune response against infection by group A streptococcal bacteria in a mammal, a human or a child using a representative number of conjugates of GASP of formula I wherein n falls in the broad size range of 'about 1 to about 50' or 'about 3 to about 30'. Additionally, the limitation 'protein fragment' encompasses a fragment of a protein that contains one or two amino acids, a dipeptide, for example. However, there is no evidence in the instant specification showing that a GASP of formula I having a molecular weight, for example, of 10 Kd or 500 Daltons, or wherein n=1 or n=2 when conjugated to such a short protein fragment would induce a 'protective' immune response in a human or a child against infection by group A streptococci.

Therefore, undue experimentation would have been required by one of ordinary skill in the art at the time the invention was made to reproducibly practice the invention due to the lack of disclosure as to the precise size of the polysaccharide of formula I that confers an average molecular weight to the polysaccharide that is large enough to be 'protective', the lack of demonstration that one or more GASP conjugates comprising the polysaccharide of formula I falling in the recited broad size range does elicit a protective immune response in a mammal, human or a child against infection by group A streptococcal bacteria, the quantity of experimentation necessary and the breadth of the claims.

16) Claims 80-93 are rejected under 35 § U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had

possession of the claimed invention.

The newly submitted claims are directed to a method of eliciting a protective immune response in a mammal against infection by group A streptococcal bacteria. However, there appears to be no descriptive support in the instant specification for the method as claimed now. Applicants state that new claim 80 is supported by original claim 26 and at page 10, lines 23-29 and page 11, lines 20-28. However, a review of the specification parts pointed to by Applicants indicates that the original claim 26 is drawn to a method of 'immunizing' a mammal against infection by group A streptococcal bacteria comprising administering to an individual an 'immunogenic amount' of a polysaccharide as recited in formula (I), wherein 'n is a number sufficient to make the group A polysaccharide large enough and of an average molecular weight to be immunogenic'. The rest of the specification parts pointed to by Applicants provide support for a method of immunizing. Therefore, the recitation of a method of eliciting a 'protective' immune response in the claims is considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P. 608.04 to 608.04(c).

Applicants are respectfully requested to point to the descriptive support in specific part(s) of the disclosure as filed, for the above-identified limitation(s), or to remove the new matter from the claims.

Objection(s)

17) Claim 80 is objected to for the reasons given below:

(a) Claim 80 is objected to for lacking a preceding article before the recitation "protein or protein fragment" (see lines 3 and 4 below the formula). To obviate the objection, it is suggested that Applicants replace the recitation with --a protein or protein fragment--.

(b) For clarity, it is suggested that in lines 2 and 3 of claim 80, Applicants replace the recitation: "polysaccharide protein conjugate or polysaccharide protein fragment conjugate" with --polysaccharide-protein conjugate or polysaccharide-protein fragment conjugate--.

Remarks

18) Claims 80-93 stand rejected.

19) Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** Applicants are reminded of the extension of time policy as set forth in 37 C.F.R 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

20) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center located in Crystal Mall 1 (CM1). The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The CM1 facsimile center's telephone number is (703) 308-4242, which receives papers seven days a week and 24 hours a day.

21) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (703) 308-9347. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

SD
S. DEVI, PH.D.
PRIMARY EXAMINER

January 2002